Name of Sponsor/Company
University of Dundee

Title of Study
Dose response of FENO to inhaled steroids in mild-to-moderate asthma

Investigator
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Study centre(s)
Asthma & Allergy Research Group, Ninewells Hospital, Dundee

Publication (reference)
ANDERSON WJ, SHORT PM, WILLIAMSON PA, **LIPWORTH BJ**. The FeNOtype Trial: Inhaled corticosteroid dose-response using domiciliary exhaled nitric oxide in persistent asthma. **Chest** 2012;142:1553-1561

Date of first enrolment
10/02/2010

Date of last completed
29/12/2011

Phase of development
Phase IV

Objectives
To characterise dose-response, as assessed by exhaled nitric oxide following administration of fluticasone propionate at 2 doses (50µg b.i.d. and 250µg b.i.d.) in mild to moderate adult asthmatics.

Methodology
A randomized, crossover trial in 21 patients with mild to moderate persistent asthma receiving ICS with elevated FeNO (30 parts per billion [ppb]) that increased further (10 ppb) after ICS washout. Patients were randomized to 2 weeks of either fluticasone propionate 50 µg bid (FP100) or 250 µg bid (FP500).

Number of patients planned
Sufficient to complete 20

Number of patients analysed
21

Diagnosis and main criteria for inclusion
Mild to moderate persistent asthma receiving ICS with elevated FeNO (30 parts per billion [ppb]) that increased further (10 ppb) after ICS washout.

Test product dose

Arm A
Fluticasone Propionate 50 µg bid (FP 100 µg) (2 weeks)

Arm B
Fluticasone Propionate 250 µg bid (FP 500 µg) (2 weeks)

Duration of treatment
4 weeks (2 treatment periods of 2 weeks)

Reference therapy
N/A

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Criteria for evaluation

Primary Endpoint
Response in diurnal domiciliary FENO levels.

Secondary Endpoints
Mannitol challenge, serum eosinophilic cationic protein (ECP), blood eosinophil count, and asthma control questionnaire.

Statistical methods
All data were examined for normality, with non-Gaussian distributions logarithmically transformed. All baselines were pooled as no significant differences were demonstrated comparing washouts.

Differences between group means were analyzed using repeated measures analysis of variance with Bonferroni correction. Paired Student *t* tests were used for differences within or between groups as change from baseline.

Summary Conclusions

Results
We found significant dose-related reductions of diurnal FENO compared with baseline – morning FENO: baseline = 71 ppb (95% CI, 61-83 ppb); FP100 = 34 ppb (95% CI, 29-40 ppb), $P < .001$; FP500 = 27 ppb (95% CI, 22-33 ppb), $P < .001$; and significant dose separation for morning, $P < .05$, and evening, $P < .001$. Time-series FENO displayed exponential decay: FP100 $R^2 = 0.913$, half-life = 69 h (95% CI, 50-114 h); FP500 $R^2 = 0.966$, half-life = 55 h (95% CI, 45-69 h), as well as diurnal variation. The Asthma Control Questionnaire showed significant improvements exceeding the minimal important difference (> 0.5) with values in keeping with controlled asthma (< 0.75) after each dose: FP100 = 0.48 (95% CI, 0.24-0.71), $P = .004$; FP500 = 0.37 (95% CI, 0.18-0.57), $P = .001$. All other secondary inflammatory related outcomes (mannitol, ECP, and eosinophils) showed significant improvements from baseline but no dose separation

Conclusion
There is a significant dose response of diurnal F ENO to ICS in patients with asthma with an elevated F ENO phenotype, which translates into well-controlled asthma. Further interventional studies are warranted using domiciliary FENO in this specific phenotype.

Date of the report: 04/08/2015